

INVASIVE MENINGOCOCCAL DISEASE

Neisseria meningitidis
REPORT IMMEDIATELY

✓ DISEASE AND EPIDEMIOLOGY

Clinical Description:

Clinical presentation of an invasive infection with *Neisseria meningitidis* may include:

- Fever
- Petechial rash
- Purpura
- Sepsis

There are different clinical manifestations of *Neisseria meningitidis*:

Bacteremia without sepsis:

- This tends to be a mild disease, often appearing as an upper respiratory disease or viral exantham (rash). Blood cultures will be positive for *Neisseria meningitidis*. This disease has a chronic state that can be mistaken for gonococcemia. Chronic bacteremia may be due to an immunologic deficiency.

Meningococcemia without meningitis:

- The patient appears septic, with leukocytosis (increased white blood cells), skin rash, generalized malaise, weakness, headache, and hypotension. Petechiae and disseminated intravascular coagulation (DIC) are also common. Meningococcemia is the most severe presentation of this disease.

Meningitis with or without meningococcemia:

- Patients present with headache, fever, and meningeal signs, along with a cloudy CSF. The presentation varies and patients may not have the above symptoms.

Meningoencephalitis manifestations:

- Patients are profoundly ill with meningeal signs and septic spinal fluid. Deep tendon and superficial reflexes are altered (absent or hyperactive). Pathologic reflexes are frequently present.

Pneumonia:

- Symptoms include cough, chest pain, chills, rales, and pharyngitis. This can be difficult to diagnose because a sputum culture could be contaminated with respiratory flora (from a carrier), and the incidence of sepsis is low (therefore blood cultures are unlikely to be of value).

Other manifestations include:

- Epiglottitis
- Urethritis
- Arthritis
- Pericarditis
- Conjunctivitis (Primary meningococcal conjunctivitis)

Patients can progress between manifestations during their course of illness.



Petechial lesions are common with this disease, but may be missed. Lesions can occur in obscure places such as the hard palate and conjunctiva, but is generally seen on the trunk and lower limbs. It is important to carefully examine the patient, as petechia can sometimes be found only in pressure points, such as under socks or underwear elastic. The petechia rash corresponds to thrombocytopenia and is an indicator of disseminated intravascular coagulopathy (DIC). Some patients may also present with a maculopapular rash, but it is transient.

Causative Agent:

Meningococcal meningitis is caused by Gram-negative diplococci, *Neisseria meningitidis*. The sides are flattened and this organism is recognizable in Gram stain by an experienced microscopist. There is a polysaccharide capsule surrounding the organism; differences in this capsule are the basis for the serogroup. This organism is fastidious in its growth requirements, but virtually all clinical microbiology laboratories can grow it in culture.

There are at least 13 serogroups of this organism: A, B, C, D, X, Y, Z, E, W-135, H, I, K, and L. In the U.S., serogroups B, C, and Y cause approximately one-third of invasive meningococcal disease cases. In recent years there has been a decrease in invasive meningococcal disease due to serogroup B in Utah.

Differential Diagnosis:

Neisseria meningitidis is an invasive bacterial disease and must be differentiated from bacteria that create similar symptoms, such as *Streptococcus pneumoniae*, Group A and B strep, and *Haemophilus influenzae*. *Neisseria* have a characteristic presence on Gram stain (Gram-negative diplococci) which can assist with discrimination, especially when antibiotics have been started prior to collection of specimens for bacterial culture.

Laboratory identification:

Neisseria meningitidis is not difficult to identify in the laboratory. Typical specimens to obtain include blood, CSF, or synovial, pleural, or pericardial fluid.

- **Culture** – Typically, meningococcal meningitis is identified via Gram stain of the CSF and subsequent culture. The morphology of the organism is sufficient to suspect meningococcal meningitis rapidly through the Gram stain. The confirmatory culture should be available the next day. One problem with culture is with patients who are treated with antibiotics PRIOR to the spinal tap. Ideally, both CSF and blood cultures should be collected before initiating antibiotic therapy. When this is not possible, both blood and CSF culture should be collected as soon as possible after the initiation of antimicrobial therapy. Cultures can be rendered sterile as soon as 2 hours after initiation of antimicrobial therapy.
- **PCR amplification (DNA detection)** – PCR amplification has the advantage of being rapid, and being less susceptible to prior antibiotic treatment than culture. PCR is highly sensitive and specific. The UPHL can take specimens for PCR testing. These tests will be sent to the Minnesota Public Health Laboratory through an agreement with the UPHL.

Latex agglutination – This is now rarely performed. The Gram stain is generally thought to be a preferable rapid test in CSF.

Treatment:

Immediate recognition and treatment of meningococcal disease is critical. Persons with suspected meningococcal disease should be treated promptly without waiting for laboratory confirmation.

Early and appropriate antibiotic treatment markedly improves the outcome of meningococcal infections. Once the diagnosis of meningococcal disease infection is seriously considered, no more than 30 minutes ideally should elapse before the administration of appropriate antibiotics.

Clinicians should consult with an infectious disease specialist or appropriate references for current therapies.

Drugs that are not effective include first-generation cephalosporins and sulfonamides.

Case fatality:

The case fatality is highly variable and depends upon the disease and availability of appropriate health care. Meningitis or pneumonia fatality is about 7-13%, whereas fatality with septicemia can be as high as 19%. Some survivors (~10-20%) will suffer from long-term sequelae such as hearing loss, mental deficits, and loss of limbs.

Reservoir:

Humans: Up to 25% of the population may carry *Neisseria meningitidis* in their nasal mucosa without symptoms. In closed populations, such as military or residential living centers, carriage rates can be much higher. Carriage can be infrequent, intermittent, or long-lasting.

Transmission:

Carriers spread the organism via the respiratory route. Transmission is relatively inefficient, and close contact is necessary.

Susceptibility:

Disease rates are high in infancy (3-5 month olds), and then decrease from adolescence through young adulthood, and rise after the age of 60 years.

Between 1991 and 1998, the rate of meningococcal disease in people aged 18-23 years has been higher than for the general population.

Individuals thought to be at higher risk include those with underlying immune deficiencies (asplenia, complement deficiency). Other risk factors include crowding (such as living in a dormitory or military barracks), tobacco smoke use or exposure and a concurrent respiratory tract infection. Outbreaks typically occur in closed settings such as

childcare, schools and colleges (especially freshmen living in dormitories), and military training camps.

Household contacts are at increased risk (from 500 to 4,000 fold higher than non-household contacts) of developing disease following exposure.

Incubation period:

The incubation period is usually 3-4 days, with a range of 1-10 days.

Period of communicability:

People are thought to be infectious until 24 hours after initiation of antibiotic therapy.

Epidemiology:

The epidemiology of meningococcal meningitis is still unclear. Various questions remain unanswered on the sporadic, episodic nature of this disease, the susceptibility of certain populations, carrier eradication, transmission, and the failure to produce a serogroup B vaccine that elicits immunity. *Neisseria meningitidis* is the second most common cause of community-acquired adult bacterial meningitis (and the leading cause in children and young adults since the availability of the Hib vaccine). People may be more likely to acquire *Neisseria meningitidis* with a co-morbidity of a viral infection.

- Carrier state – One of the unusual features of *Neisseria meningitidis* is that it can be carried in the throats of perfectly healthy individuals. However, there is a positive relationship between the rate of carriage (or possibly transmission, not carriage) in a population, and the onset, rise, and decline of an epidemic. Other respiratory diseases usually cause no change or a decrease in the carriage rate of *Neisseria meningitidis*.

Carriers fall into three groups – chronic, intermittent, and transient. Chronic carriers can be colonized for up to 2 years. The carrier state appears to immunize the carrier.

- Invasive disease – There is a correlation between the capsular phase variation, bacterial invasion, and disease outbreaks. People with invasive disease are more likely to have been recently colonized; disease is thought to occur within the first week of acquisition.
- Outbreaks - Shifts in the age distribution can forecast the onset of an epidemic situation. Epidemics tend to occur in 5-19 year olds. Less than 5% of meningococcal meningitis cases are due to outbreaks. Outbreaks are most likely to occur in childcare settings, military recruit camps, schools, and colleges.

Approximately 800-1,500 cases of meningococcal disease occur annually in the U.S., a rate of 0.3-0.5/100,000 population. In the U.S., serogroups C and Y are the most prevalent, each causing approximately 33% of the reported invasive disease. There is some seasonality associated with this disease – it is most common in winter and spring.

Recent Utah data shows a gradual shift over the past 5 years away from serogroup B and towards serogroup Y.

Epidemic potential is related to serogroup. Epidemics are most likely among the poorest socioeconomic groups, with crowding and lack of sanitation common.

Typical Causes of Epidemic Invasive Disease (Worldwide)		
Serogroup	Where	Attack Rate
A	Less developed countries	Up to 500 cases per 100,000 population
B	Developed countries	50-100 case per 100,000 population
C	Developed and undeveloped countries	Up to 500 cases per 100,000 population

✓ PUBLIC HEALTH CONTROL MEASURES

Public health responsibility:

Public health has the primary responsibility for identifying and chemoprophylaxing contacts to identified cases. Other important public health responsibilities include:

- Investigating cases to determine possible linkage to other cases in Utah or beyond.
- Collecting demographic information to identify “at risk” populations.
- Encouraging “at risk” populations to receive immunization.
- Monitoring levels of disease in the community.
- Analyzing disease trends.
- Tracking age distribution and types of invasive meningococcal disease reported to public health, to determine whether a transition from a non-epidemic to an epidemic period is occurring. (Remember that epidemic periods predominantly affect those in the 5-19 year age range.)
- Monitor reported serogroups, and collecting and reporting sufficient information to determine whether there is a changing pattern and whether vaccine is covering the majority of reported cases.

Prevention:

Prevention methods for meningococcal disease include: vaccination, chemoprophylaxis of close contacts following identification of an index case, use of droplet precautions. See the following sections for more information regarding chemoprophylaxis and vaccine.

Droplet precautions should be continued for 24 hours after institution of effective antibiotics in patients with suspected or confirmed *Neisseria meningitidis* infections.

Chemoprophylaxis:

If the patient has a positive culture for *Neisseria meningitidis*, then all close contacts should be prophylaxed with antibiotics. See section “[Identification of case contacts](#)” for information on determining what people are considered close contacts of the case.

Prophylaxis is not indicated if exposure to the case is brief. This includes a majority of healthcare workers unless there was direct exposure to respiratory secretions (as with suctioning or intubation).

Additionally, prophylaxis is not recommended for close contacts of patients with evidence of *Neisseria meningitidis* only in non-sterile sites such as an oropharyngeal swab, endotracheal secretions, or conjunctival swab. Reports of secondary cases after close contact to persons with noninvasive pneumonia or conjunctivitis are rare.

If the patient was treated with antibiotics before the culture was obtained, and no bacteria are found, then the decision to administer prophylaxis to close contacts becomes more difficult. Each situation should be reviewed individually to determine the likelihood of invasive meningococcal disease. The State Epidemiologist can assist with this review process.

- **Antibiotics** - Prophylaxis typically consists of
 - Rifampin
 - Adults: 600 mg q 12h for 2 days;
 - Children <1 month, 5 mg/kg q12h for 2 days;
 - Children >1 month, 10 mg/kg q12h <maximum 600 mg/day> orally for 2 days);
 - Resistance is known to occur during prophylaxis with rifampin.
 - Ciprofloxacin
 - Adults: 500 mg single dose, or
 - Ceftriaxone
 - Adults 250 mg single IM dose;
 - Children <15 years, 125 mg, single IM dose).

Note: rifampin and ciprofloxacin are not recommended for pregnant or possibly pregnant women.

Penicillin and sulfonamides are not appropriate drugs for prophylaxis.

Timing of prophylaxis – The rate of secondary disease in contacts is highest immediately after onset of disease in the index patient. Because of this, antibiotic prophylaxis should be administered as early as possible (ideally <24 hours after identification of the index patient). Antibiotic prophylaxis administered >14 days after exposure to the index patient is not recommended.

Vaccine:

Widespread vaccination of contacts would not be advised except during outbreaks. Ensure that the vaccine covers the serogroup of the circulating bacteria before implementing this strategy in an outbreak setting.

Types of vaccine

- Meningococcal Polysaccharide Vaccine (MPSV4) – available since the 1970's. It is the only meningococcal disease vaccine licensed for people older than 55 years.
- Meningococcal Conjugate Vaccine (MCV4)
 - Menactra – approved for use in persons 9 months through 55 years of age.
 - Menveo – approved for use in person 2 years through 55 years of age.

Both MPSV4 and MCV4 can prevent 4 types (A, C, Y, and W-135) of meningococcal disease, including 2 of the 3 types most common in the U.S.

Vaccination recommendations

- Routine Vaccination
 - Two doses of MCV4 are recommended for adolescents 11-18 years of age. First dose at 11-12 years, plus a booster at age 16.
 - If the first dose is given between 13-15 years of age, the booster should be given between 16-18 years of age.
 - If the first dose is given after the age of 16, a booster is not needed.
- People at increased risk
 - College freshmen living in dormitories.
 - Laboratory personnel who are routinely exposed to meningococcal bacteria.
 - U.S. military recruits.
 - Anyone traveling to, or living in, a part of the world where meningococcal disease is common, such as parts of Africa.
 - Anyone who has a removed or damaged spleen.
 - Anyone who has persistent complement component deficiency.
 - People who might have been exposed to meningitis during an outbreak.

A complete table with all Meningococcal Disease vaccination recommendations by age and/or risk factor is available at <<http://www.immunize.org/catg.d/p2018.pdf>>

Isolation and quarantine requirements:

Isolation: Patients should be on respiratory isolation until 24 hours after starting antibiotic therapy.

Hospital: Patients should be on respiratory isolation until 24 hours after starting antibiotic therapy.

Quarantine: Not applicable.

CASE INVESTIGATION

Reporting:

All cases of invasive meningococcal disease are immediately reportable in Utah. This disease should be reported when suspected, not just when confirmed.

CSTE Reporting Swimlanes

Criterion	Reporting		
<i>Clinical Evidence</i>			
Petechial Rash	O		
Purpura	O	N	
Sepsis	N		
Death		N	
Healthcare record contains a diagnosis of meningococcal disease			S
Death certificate lists meningococcal disease as a cause of death or a significant condition contributing to death			S
Medical examiner case of person found dead with purulent exudate on meninges			S
Medical examiner case of person found dead with purpuric rash and/or hemorrhagic organs (particularly adrenals)			S
<i>Laboratory Evidence</i>			
Isolation of <i>Neisseria meningitidis</i> from a normally sterile site			S
Evidence of <i>N. meningitidis</i> DNA using a validated polymerase chain reaction (PCR) obtained from a specimen collected from a normally sterile site			S
<i>N. meningitidis</i> antigen identified by immunohistochemistry (IHC) on formalin-fixed tissue			S
<i>N. meningitidis</i> antigen identified in CSF by latex agglutination			S
Gram-negative diplococci from a normally sterile site			S

Notes:

S = This criterion alone is sufficient to identify a case for reporting.

N = All “N” criteria in the same column are necessary to identify a case for reporting.

O = At least one of these “O” (Optional) criteria in each category (i.e., clinical evidence and laboratory evidence) in the same column – in conjunction with all “N” criteria in the same column – is required to identify a case for reporting. (These optional criteria are alternatives, which means that a single column will have either no O criteria; no column should have only one O.)

Case definition:
Meningococcal Disease (2015):

Suspected:

- Clinical purpura fulminans in the absence of a positive blood culture; or
- Gram-negative diplococci, not yet identified, isolated from a normally sterile body site (e.g., blood or CSF)

Probable

- Detection of *N. meningitidis* antigen
 - In formalin-fixed tissue by immunohistochemistry (IHC); or
 - In CSF by latex agglutination

Confirmed

- Detection of *N. meningitidis*-specific nucleic acid in a specimen obtained from a normally sterile body site (e.g., blood or CSF), using a validated polymerase chain reaction (PCR) assay; or
- Isolation of *N. meningitidis*
 - From a normally sterile body site (e.g., blood or CSF, or less commonly, synovial, pleural, or pericardial fluid); or
 - From purpuric lesions.

Clinical Criteria

Clinical purpura fulminans in the absence of a positive blood culture

Laboratory Criteria

- Gram-negative diplococci, not yet identified, isolated from a normally sterile body site (e.g., blood or CSF)
- Detection of *N. meningitidis* antigen
 - In formalin-fixed tissue by immunohistochemistry (IHC); or
 - In CSF by latex agglutination
- Detection of *N. meningitidis*-specific nucleic acid in a specimen obtained from a normally sterile body site (e.g., blood or CSF), using a validated polymerase chain reaction (PCR) assay; or
- Isolation of *N. meningitidis*
 - From a normally sterile body site (e.g., blood or CSF, or less commonly, synovial, pleural, or pericardial fluid); or
 - From purpuric lesions.

Epidemiologic Linkage

Not applicable for case classification.

CSTE Case Classification Swimlanes

Criterion	Case Definition			
	Suspected		Probable	Confirmed
<i>Clinical Evidence</i>				
Purpura fulminans	N			
<i>Laboratory Evidence</i>				
Isolation of <i>Neisseria meningitidis</i> from a normally sterile body site				S
Isolation of <i>Neisseria meningitidis</i> from a purpuric lesion				S
Detection of <i>N. meningitidis</i> -specific nucleic acid in a specimen obtained from a normally sterile body site using a validated polymerase chain				S
Detection of <i>N. meningitidis</i> antigen in formalin-fixed tissue by immunohistochemistry (IHC)			S	

Detection of <i>N. meningitidis</i> antigen in CSF by latex agglutination			S	
Identification of Gram-negative diplococci in a specimen from a normally sterile body site		S		

Notes:

S = This criterion alone is sufficient to classify a case

N = All "N" criteria in the same column are necessary to classify a case

Case Investigation Process:

- Confirm the diagnosis (if patient does not have a confirmed diagnosis, but the clinician determines that the disease was likely to be due to bacterial meningitis, then it may be prudent to continue with chemoprophylaxis).
- Determine who is at risk. People thought to be at highest risk include household, childcare, and nursery school contacts. In addition, close contacts include people who have had contact with the patient's oral secretions, such as kissing, sharing toothbrushes, sharing utensils, sharing food (food that might have oral secretions, not just eating at the same table), and people who frequently ate or slept in the same dwelling as the patient. The patient is infectious during the following period of time:
 - From 7 days before the onset of their disease UNTIL
 - Successful completion of 24 hours of antibiotics.
- You should identify all close contacts to the patient that occurred during the above risk period.
- Notify UDOH.
- Ensure that contacts are offered prophylaxis:
 - Ideally, this should occur within 24 hours after the case is identified.
 - Prophylaxis given more than 14 days after the onset of illness in the index case is of limited or no value.
- All close contacts should be observed for 10 days following exposure. If any febrile illness develops, contacts should receive immediate medical attention.
- For patients on airline flights lasting more than 8 hours, passengers sitting directly next to the patient are candidates for prophylaxis.
- Health care workers are low risk UNLESS they provided mouth-to-mouth resuscitation or have unprotected contact during endotracheal intubation during 7 days prior to onset of disease OR after disease onset, but before 24 hours of antimicrobial therapy being completed.
- Consider starting enhanced surveillance for additional cases of illness.
- Ensure that the organism is serogrouped. Contact the diagnosing laboratory, and have the laboratory send the specimen to the Utah Public Health Laboratory for serogroup testing.
- If more than one case is found:
 - Notify the UDOH bacterial disease epidemiologist and request assistance if needed.
 - Investigate for possible links between cases
 - Determine if the outbreak is limited to an organization (e.g. childcare, school) or is community-wide.

- Determine the target group for vaccination.
 - Consider enhanced surveillance or special case-finding methods.
- Ensure that information essential to trend analysis is completely filled out before the investigation is closed. Examples of such information would be: onset date, was patient hospitalized, how long was patient hospitalized, did patient die, etc.

Outbreaks:

An outbreak will be defined as:

- More than two cases in a closed population in a 30 day period;
- Two or more cases with direct epidemiological linkage; or
- More than two cases of PFGE-identical isolates in a 30 day period.

Identification of case contacts:

Case contacts are those that:

- Live in the same household (especially young children), this includes roommates.
- Share the same sleeping space (such as military barracks or dorm rooms) during 7 days prior to illness onset and until 24 hours after initiation of appropriate antibiotic.
- Contacts at daycare or nursery during 7 days prior to illness onset and until 24 hours after initiation of appropriate antibiotic.
- Any intimate contact of case during 7 days prior to illness onset and until 24 hours after initiation of appropriate antibiotic.
- Close social contacts (through kissing, sharing water bottles, cutlery, or very close friends) that have had contact with the case during 7 days prior to illness onset and until 24 hours after initiation of appropriate antibiotic.
- Medical personnel, if they had unprotected exposure to patient secretions (e.g. mouth to mouth resuscitation, endotracheal intubation, endotracheal tube management) during 7 days prior to illness onset OR after illness onset but before patient has received 24 hours of appropriate antibiotic therapy.
- Travelers who have had direct contact with respiratory secretions of a case or who were seated directly next to a case on a prolonged flight (lasting ≥ 8 hours).

Case contact management:

People who meet the criteria for case contacts should have:

- Prophylactic antibiotics.
 - Throat or nasopharyngeal cultures are of no value in determining who should receive prophylaxis.
- Be under fever surveillance.
 - Initiate appropriate antibiotic therapy for individuals with preliminary signs of disease.

✓ REFERENCES

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